DETAILED ACTION

1. Applicant's election with traverse of Group I, encompassing claims 39-42, 45-49 and 52-55 and drawn to a method for the treatment of a psychiatric disorder, disease or condition comprising administering Copolymer 1 or a Copolymer 1-related peptide or polypeptide, in the reply filed on June 16, 2011 is acknowledged. The traversal is on the ground(s) that as amended, the claims now exclude Alzheimer's disease from the claimed diseases and therefore the prior art reference by Schwartz (2001) no longer reads upon the claimed invention to break unity of invention as per PCT Rule 13.2.

While the examiner agrees that the Schwartz reference no longer reads upon the presently recited invention, the newly identified art discussed below (WO 01/52878) does read upon the present claims and could be used to establish a lack of unity *a priori* under PCT Rule 13.2. Regardless, because the reference teaches the inventions of both Groups I and II, the examiner has decided not to impose another restriction requirement between groups I and II, and to examine both groups together. Accordingly claim 43 has been rejoined for examination.

2. With respect to the species election requirement, Applicant's election with traverse of the species of schizophrenia and related disorders, as in claims 48 and 49, in the reply filed on June 16, 2011 is acknowledged. The traversal is on the ground(s) that PCT Rule 13.1 does not provide for species election, and since the amended generic claim 39 includes sufficiently few that a search and examination of all the species at one time would no impose a serious burden on the examiner. This is not found persuasive because this application is a 371 national stage application, and

therefore is subject to Unity of Invention consideration under PCT Rule 13.1 and 13.2 (see MPEP § 1800) and not U.S. restriction practice such as for applications filed under 35 U.S.C. 111. Therefore, whether or not an undue burden for examination exists is not considered relevant to the instant situation because search burden is not a factor used to determine unity of invention or lack thereof. The basis for the lack of unity in the instant application was set forth in the restriction requirement mailed March 16, 2011. Specifically, because the different psychiatric diseases, disorders or conditions are each unique in their diagnosis, etiology, pathology, affected populations, and even in animal models used to study the human conditions, the different species do not relate to a *general inventive concept*, which is the basis for determining unity of invention under PCT Rule 13.1, and under PCT Rule 13.2, the different species lack the same or corresponding special technical feature as noted above. Therefore, the species election requirement is maintained.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 45-47 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on June 16, 2011.

4. Claims **39-43, 48, 49** and **52-55**, to the extent they read upon the elected species of schizophrenia and related disorders, are under examination in the current office action.

Information Disclosure Statement

5. The information disclosure statements (IDSs) submitted on June 8, 2006, October 2, 2009 and March 3, 2011 have been considered and the references therein are of record.

Claim Objections

6. Claim 45 is objected to because of the following informalities: the right parenthesis ")" following "PTSD" in line 5 appears to have been inadvertently deleted in the claim amendment. Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the fourth paragraph of 35 U.S.C. 112:

Subject to the [fifth paragraph of 35 U.S.C. 112], a claim in dependent form shall contain a reference to a claim previously set forth and then specify a further limitation of the subject matter claimed. A claim in dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers.

8. Claim 40 is rejected under 35 U.S.C. 112, 4th paragraph, as being of improper dependent form for failing to further limit the subject matter of the claim upon which it depends, or for failing to include all the limitations of the claim upon which it depends.

In the instant case, claim 40 recites that the administering step comprises *immunizing* an individual. The present specification, however, makes no distinction between "administering" and "immunizing" *per se*, and the terms are often used interchangeably throughout the disclosure. In other words, in all cases of therapeutic administration of the claimed agents, the goal is to immunize the individual. Therefore, it is unclear how the step of "immunizing" of claim 40 limits the "administering" of claim 39. Applicant may cancel the claim(s), amend the claim(s) to place the claim(s) in proper dependent form, rewrite the claim(s) in independent form, or present a sufficient showing that the dependent claim(s) complies with the statutory requirements.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 39-43, 49 and 52-55 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 01/52878 by Eisenbach-Schwartz et al. (published Jul. 26, 2001), as evidenced by the Wikipedia entry for "Aluminum hydroxide", downloaded Aug. 18, 2011.

Eisenbach-Schwartz et al. teach a method of treating injury to, or diseases of, the central nervous system comprising administering Copolymer 1 (Cop 1), a Cop 1-related peptide or polypeptide, or activated T cells that recognize an antigen of Cop 1 or a Cop1-related peptide or polypeptide (see abstract). Eisenbach-Schwartz teaches that

in one embodiment, Cop 1 or a Cop 1-related peptide or polypeptide is administered in methods for protecting CNS cells from glutamate toxicity or for treating injury or disease caused or exacerbated by glutamate toxicity (see p. 24, lines 25-29). In particular, Eisenbach-Schwartz notes that in light of the findings with respect to the glutamate protective aspect of the disclosed invention, clinical conditions that may be treated in accordance with the disclosed invention include anxiety and psychosis (see p. 34, lines 5-9). Eisenbach-Schwartz further comments that protection against glutamate toxicity can also be achieved using Cop 1-related T cell treatment (see p. 34, lines 17-20). Hence, the reference teaches treating a patient having psychosis comprising administering Cop 1, a Cop 1-related peptide or polypeptide, or T cells activated by Cop 1 or a Cop 1-related peptide or polypeptide, which is on point to claims 39 and 49 with respect to treatment of a schizophrenia related disorder, such as a brief psychotic disorder. A brief psychotic episode is, after all, a short, non-recurring period of psychosis. These teachings are also on point to the specific agents as recited in present claims 41-43.

With respect to claims 40 and 52-55, Eisenbach-Schwartz discloses that pharmaceutical compositions comprising Cop 1 or Cop 1-related peptide or polypeptide may optionally be administered with an adjuvant, such as alum, in the usual manner for immunization (see p. 40, lines 1-5). Note that the term alum, particularly when used as an adjuvant in vaccine preparations, is a generic name for aluminum hydroxide, which is safe for human clinical use. (See 1st paragraph of page 4 of Wikipedia entry for "Aluminum hydroxide", which notes that “[a]luminum hydroxide is often mis-called

“alum" even by researchers”.) Because Eisenbach-Schwartz teaches that the use of an adjuvant is optional, this would account for administration of Cop 1 without an adjuvant, as in claim 53. Accordingly, the teachings of Eisenbach-Schwartz provide for the presently recited invention of claims 39-43, 49 and 52-55.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claim 48 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO 01/52878 by Eisenbach-Schwartz et al. (published Jul. 26, 2001) in view of Farber et al. (*Mol Psychiatry*, 2002; 7(1):32-43).

The teachings of Eisenbach-Schwartz have been discussed above. Briefly, the WO document teaches that because of the capacity of Copolymer 1 (Cop 1) to protect CNS neurons from glutamate toxicity, individuals having psychosis may be treated by administration of a therapeutically effective amount of Cop 1 (see p. 24 lines 25-29 and p. 34 lines 6-9). The difference, therefore between the teachings of Eisenbach-Schwartz and the presently claimed invention is that the prior art reference does not teach that the psychosis is schizophrenia.

Farber et al. teach that NMDA receptor hypofunction (NRHypo)-induced neurotoxicity may underlie neurodegeneration and psychosis in diseases such as Alzheimer's disease and schizophrenia (see abstract). The NMDA receptor is, of course, a receptor for glutamate and thus is responsible for excitatory glutamatergic signaling in the CNS.

It would have been obvious to one of ordinary skill in the art at the time the invention was filed to have modified the teachings of Eisenbach-Schwartz to treat patients having schizophrenia by administering Cop 1. The skilled artisan would have been aware of the teachings of Eisenbach-Schwartz, for example, which state that psychosis can be treated by using Cop 1 because of the neuroprotective effects of Cop

1 against glutamate toxicity. In view of the teachings of Farber et al., the ordinary skilled artisan would have also recognized that schizophrenia, which is a specific type of psychosis, is associated with glutamate receptor-induced neurodegeneration (i.e., glutamate-related neurotoxicity). Therefore, it would have been obvious to use an agent (Cop 1) taught be useful in abrogating glutamate toxicity for the treatment of psychosis for the treatment of such pathology in schizophrenia. This is because the skilled artisan has good reason to pursue the known options within his or her technical grasp to yield predictable results. Particularly in view of the fact that psychosis is the main component of schizophrenia, such would amount to the simple substitution of one know element (i.e., psychosis) for another (i.e., schizophrenia) to obtain predictable results.

14. Claims 39-43, 48, 49 and 52-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wank (*Med Hypotheses*, 2002; 59(2):154-158) in view of Ziemssen et al. (*Brain*, 2002 Nov; 125:2381-2391) and WO 01/52878 by Eisenbach-Schwartz et al. (published Jul. 26, 2001) as evidenced by the Wikipedia entry for "Aluminum hydroxide", downloaded Aug. 18, 2011.

Wank teaches that schizophrenia and other psychiatric disorders can be treated by adoptive immunotherapy. In particular, Wank discloses that activation of all T lymphocytes reactivates those downregulated by low-grade chronic infections and restores equilibrium in immune cell populations. Further, different immune cell subpopulations express different neurotrophin receptors and produce different neurocytokines, particularly brain-derived neurotrophic factor (BDNF) and neurotrophin-

3 (NT-3), which Wank notes appear to play important roles in schizophrenia and bipolar disorder (see abstract).

Wank teaches that adoptive immununotherapy involves stimulating a patient's immune cells *ex vivo*, such as by activation of the pan-T cell receptor complex cofactor CD3. The CD3-activated T lymphocytes are then injected back into the patient, allowing for greater crosstalk to the CNS by producing anti-inflammatory cytokines and neurotrophins such as BDNF and NT-3 (see p.155, left column, and Fig. 2 on p. 156). Therefore, Wank proposes that adoptive immunotherapy is effective in the treatment of psychiatric disorders. Moreover, Wank demonstrates that this immunotherapeutic approach was capable of producing substantial and sustained improvements in a patient having schizophrenia (see case study on p. 157). The difference between the teachings of Wank and the presently claimed invention is that Wank does not teach that the activated administered T cells were stimulated by Copolymer 1 or a Cop 1-related peptide or polypeptide, or that the activation of T cell occurs in vivo by immunizing the patient with a vaccine comprising Cop 1 or a Cop 1-related peptide or polypeptide, with or without an adjuvant.

Ziemssen et al. teach that glatiramer acetate (GA; also known as Copolymer 1), which is a pan T-helper (TH) cell activator, induces T cells to produce BDNF. Ziemssen thus comments that the beneficial effects of GA-activated T cells might be due to their release of BDNF at the site of neuronal injury.

Eisenbach-Schwartz et al. teach a method of treating injury to, or diseases of, the central nervous system comprising administering Copolymer 1 (Cop 1), a Cop 1-related

peptide or polypeptide, or activated T cells that recognize an antigen of Cop 1 or a Cop1-related peptide or polypeptide (see abstract). Eisenbach-Schwartz teaches that in one embodiment, Cop 1 or a Cop 1-related peptide or polypeptide is administered in methods for protecting CNS cells from glutamate toxicity or for treating injury or disease caused or exacerbated by glutamate toxicity (see p. 24, lines 25-29). In particular, Eisenbach-Schwartz notes that in light of the findings with respect to the glutamate protective aspect of Cop 1 therapy, psychosis may be treated in accordance with the disclosed invention (see p. 34, lines 5-9). Eisenbach-Schwartz further comments that protection against glutamate toxicity can also be achieved using Cop 1-activated T cell treatment (see p. 34, lines 17-20). Hence, the reference teaches treating a patient having psychosis comprising administering Cop 1, a Cop 1-related peptide or polypeptide, or T cells activated by Cop 1 or a Cop 1-related peptide or polypeptide, which is on point to claims 39 and 49 with respect to treatment of a schizophrenia related disorder, such as a brief psychotic disorder. A brief psychotic episode is, after all, a short, non-recurring period of psychosis. These teachings are also on point to the specific agents as recited in present claims 41-43.

With respect to claims 40 and 52-55, Eisenbach-Schwartz discloses that pharmaceutical compositions comprising Cop 1 or Cop 1-related peptide or polypeptide may optionally be administered with an adjuvant, such as alum, in the usual manner for immunization (see p. 40, lines 1-5). Note that the term alum, particularly when used as an adjuvant in vaccine preparations, is a generic name for aluminum hydroxide, which is safe for human clinical use. (See 1st paragraph of page 4 of Wikipedia entry for

"Aluminum hydroxide", which notes that “[a]luminum hydroxide is often mis-called “alum" even by researchers”.) Because Eisenbach-Schwartz teaches that the use of an adjuvant is optional, this would account for administration of Cop 1 without an adjuvant, as in claim 53.

It would have been obvious to one of ordinary skill in the art at the time the present invention was filed to have modified the adoptive immunotherapeutic approach for the treatment of schizophrenia as taught by Wank by instead administering Cop 1-activated T cells or else a vaccine comprising Cop 1 or a Cop 1-related peptide or polypeptide, as taught by Eisenbach-Schwartz. Based upon the teachings of Wank, the skilled artisan would have recognized that adoptive immunotherapy could be used successfully to treat a patient having schizophrenia, and that part of the beneficial effects using this approach may be derived from the ability of the activated T cells to produce anti-inflammatory cytokines and neurotrophins such as BDNF within the brain. Based on the teachings of Ziemssen, the skilled artisan would have recognized that glatiramer acetate (Cop 1) induces activated T cells to produce BDNF, particularly within the CNS. And based upon the teachings of Eisenbach-Schwartz, the ordinary skilled artisan would have known that psychosis, which is a condition commonly caused by schizhophrenia, may be treated by immunizing a patient with Cop 1, a Cop 1-related peptide or polypeptide, or by administering Cop 1-activated T cells. Thus, it would appear that Cop 1, which is well tolerated and already approved for human clinical use, could be used in the manner taught by Wank for adoptive immunotherapy comprising the administration of activated T cells. Additionally, it would have been obvious to

simply administer Cop 1 or a Cop 1-related peptide or polypeptide according to the teachings of Eisenbach-Schwartz, because this is technically simpler than a method involving the removal, *ex vivo* stimulation, and re-injection of activated T cells to a patient, whilst producing similar efficacy. The artisan would have had a reasonable expectation that such a method could be successfully used to treat schizophrenia or a related disorder based upon the demonstration of Wank using a similar immunotherapeutic approach to treat patients having schizophrenia, bipolar disorder and autism. Accordingly, the combined teachings of the above references render obvious the presently recited invention of claims 39-43, 48, 49 and 52-55.

Double Patenting

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422

F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. Claims 39-42, 49 and 52-55 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 5, 6, 9, 10 and 15 of copending Application No. 12/437,167. Although the conflicting claims are not identical, they are not patentably distinct from each other because in each case the claims recite immunizing an individual with Copolymer 1 or a Copolymer 1-related peptide or polypeptide so as to treat psychosis. Further, claims 5 and 6 of the copending ‘167 application recite that the agents may be used with or without an adjuvant for immunization. One of skill in the art would have recognized that for vaccine preparations, there are only a few adjuvants that are safe for human clinical use, such as aluminum hydroxide. Therefore, the limitations of present claims 54 and 55 are rendered obvious by the claims of the ‘167 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

17. Claims 39-43, 49, 52 and 53 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 31 and 33 of U.S. Patent No. 6,844,314. Although the conflicting claims are not identical, they are not patentably distinct from each other because in each case the claims recite the administration of an immunizing composition of Copolymer 1, a Copolymer 1-related peptide or polypeptide, or T cell that have been activated by Copolymer 1 or a Copolymer 1-related peptide or polypeptide to an individual for therapy. In particular, claim 33 of the patent recites that the disease, disorder or condition to be treated is one whose secondary neurodegenerative effects are caused or exacerbated by glutamate toxicity.

MPEP § 804 (II)(B)(1) states that those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent. *In re Vogel*, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970). The court in *Vogel* recognized "that it is most difficult, if not meaningless, to try to say what is or is not an obvious variation of a claim," but that one can judge whether or not the invention claimed in an application is an obvious variation of an embodiment disclosed in the patent which provides support for the patent claim. According to the court, one must first "determine how much of the patent disclosure

pertains to the invention claimed in the patent" because only "[t]his portion of the specification supports the patent claims and may be considered." The court pointed out that "this use of the disclosure is not in contravention of the cases forbidding its use as prior art, nor is it applying the patent as a reference under 35 U.S.C. 103, since only the disclosure of the invention claimed in the patent may be examined."

In the instant case, the ‘314 patent discusses that diseases, disorders or conditions that have secondary neurodegenerative effects caused or exacerbated by glutamate toxicity include psychosis (see column 18, lines 27-31). Accordingly, the patented claims render obvious the instantly recited invention of claims 39-43, 49, 52 and 53.

Conclusion

18. No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly A. Ballard whose telephone number is (571)272-2150. The examiner can normally be reached on Monday-Friday 8:30 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Daniel Kolker can be reached on 571-272-3181. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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